

REMARKS

I. Status of the Claims

Claims 1-21 are pending. Claims 20 and 21 were previously withdrawn. Claims 1-7, 9-15, and 17-19 stand rejected, while the Examiner objects to claims 8 and 16. Applicants have amended claim 1 to correct a minor typographical error. Applicants have also amended claim 1 by inserting "e)" before the phrase "a sequence that hybridizes after three washes at 65 °C." Applicants have also amended claims 8 and 16 to independent form, and have included the elements from the claims from which those claims formerly depended.

II. Claims 1-7, 9-15, and 17-19 Are Not Anticipated

The Examiner rejects claims 1-7, 9-15, and 17-19 under 35 U.S.C. § 102(b) as allegedly anticipated by WO99/65924 ("the '924 application"). Office Action, p. 4. The Examiner asserts that "at least one of the polynucleotides of the '924 invention is fully complementary to nucleotides 752-761 of SEQ ID NO: 7 of the instant invention and thus will hybridize with either of SEQ ID NOs: 3-7 of the instant invention." *Id.* at 5. The Examiner states that additional sequences in the '924 application are identical over different regions spanning ten nucleotides that would allegedly hybridize under the conditions recited in the claims. *Id.* The Office also asserts that the burden is on Applicant to demonstrate that the sequences of the '924 application do not exhibit the function of the claimed nucleotides. *Id.* at 6-7.

Applicants traverse. The sequences of the '924 application do not anticipate the claimed sequences at least because they would not hybridize under the conditions recited in the claims. Thus, the full-length sequences of the '924 application do not

anticipate because they do not disclose all the elements of the claims. See MPEP § 2131 (8th ed., 5th rev. 2007).

“For oligonucleotides shorter than 18 nucleotides, the T_m of the hybrid can be estimated by multiplying the number A+T residues in the hybrid by 2 °C and the number of G+C residues by 4 °C and adding the two numbers.” Sambrook, Fritsch, & Maniatis, Molecular Cloning, Second Edition, page 11.46 (1989). When this equation is applied to the hybrids that could potentially form between the sequences of the '924 application and the claimed sequences the following results are obtained:

'924 Sequence	A/T Content	G/C Content	T_m (°C)
# 1	$4 * 2 = 8$	$6 * 4 = 24$	$8 + 24 = 32$
# 2	$2 * 2 = 4$	$8 * 4 = 32$	$4 + 32 = 36$
# 3	$3 * 2 = 6$	$7 * 4 = 28$	$6 + 28 = 34$

The claims recite hybridization at 65 °C, which is substantially above the T_m of the hybrids that could form between the claimed nucleotide sequences and the ten base pair sequences of the '924 application. Accordingly, the sequences of the '924 application would not hybridize to the claimed sequences under the recited hybridization conditions, and the '924 application cannot anticipate the claimed polynucleotides.

Applicants also disagree that the 10 base pair fragments of the '924 application would necessarily have the properties of the claimed nucleotides as required for a rejection according to M.P.E.P § 2112 based on inherency. There is nothing to suggest that the 10 base pair sequences of the '924 application have the same function as the claimed sequences. In fact, all three of the sequences of the '924 application are

derived from SAGE analysis, which generates sequences from expressed transcripts, not promoters. As stated on each of the Results provided by the Office, the sequences

represent SAGE (serial analysis of gene expression) tags used to identify mRNA transcripts encoding immunostimulatory co-factor proteins which are preferentially or differentially expressed in monocyte-derived dendritic cells compared with monocytes. Some of the transcripts correspond to known genes or ESTs.

See Sequence Search Alignments Nos. 1-3 provided with Office Action mailed October 4, 2007.

Thus, the 10 bp sequences of the '924 application appear to correspond to mRNAs that encode immunostimulatory co-factor proteins, not sequences that induce gene expression. Accordingly, Applicants respectfully submit that the Examiner has failed to provide a "sound basis for believing that the products of the applicant and the prior art are the same," which would justify shifting the burden to Applicants to show that they are not. M.P.E.P § 2112.01.

Applicants respectfully submit that the '924 application does not anticipate claims 1-7, 9-15, and 17-19, and request that the Examiner withdraw the rejection.

III. Claim Objections

The Examiner objects to claims 8 and 16 as dependent upon a rejected base claim, but states that these claims "would be allowable if rewritten to remove the nonelected subject matter and rewritten in independent form to include all of the limitations of the base claim and any intervening claims." Office Action, p. 9.

Applicants have amended claims 8 and 16 as suggested by the Examiner and respectfully request that the Examiner withdraw the objections.

CONCLUSION


In view of these amendments and remarks, Applicants submit that the application is in condition for allowance.

Please grant any extensions of time required to enter this paper and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

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Molecular Cloning

A LABORATORY MANUAL

SECOND EDITION

Sambrook • Fritsch • Maniatis

Molecular Cloning

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SECOND EDITION

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CALCULATING MELTING TEMPERATURES FOR PERFECTLY MATCHED HYBRIDS BETWEEN OLIGONUCLEOTIDES AND THEIR TARGET SEQUENCES

When using single oligonucleotides that match the target sequence perfectly, hybridization conditions can easily be derived from the calculated T_m of the hybrid. For oligonucleotides shorter than 18 nucleotides, the T_m of the hybrid can be estimated by multiplying the number of A + T residues in the hybrid by 2°C and the number of G + C residues by 4°C and adding the two numbers (Itakura et al. 1984). However, this method overestimates the T_m of hybrids involving longer oligonucleotides.

A different approach has been taken by E. Fritsch (unpubl.), who found that the equation originally used to calculate the relationship between G + C content, ionic strength of the hybridization solution, and the T_m of long DNA molecules (Bolton and McCarthy 1962):

$$T_m = 81.5 + 16.6(\log_{10}[\text{Na}^+]) + 0.41(\text{fraction G + C}) - (600/N),$$

where N = chain length, predicts reasonably well the T_m for oligonucleotides as long as 60–70 nucleotides and as short as 14 nucleotides.

This formula only works for Na^+ concentrations of 1 M or less.